CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-272

STATISTICAL REVIEW(S)

STATISTICAL REVIEW AND EVALUATION

Biometrics Division: VI (HFD-705)

NDA NO.:	22-272
SERIAL NO.:	S_000
DATE RECEIVED BY THE CENTER:	May 13, 2008, June 15, 2009
DRUG NAME:	Oxycodone HCL 10, 15, 20, 30, 40, 60, and 80 mg TR
DOSAGE FORM:	Tablets
INDICATION:	Pain management
SPONSOR:	Purdue Pharma, L.P.
DOCUMENTS REVIEWED:	Electronic Copy Dated May 13, 2008, June 15, 2009
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EXECUTIVE SUMMARY OF STATISTICAL FINDINGS

1.1 Conclusions and Recommendations

The sponsor submitted a 24-month stability studies for (b) (4) 100, (b) (4) count bottles of Oxycodone HCL 10, 15, 20, 30 and 40 mg TR Tablets with the request for an extrapolated shelf life of 24 months on May 13, 2009. The sponsor also submitted a 24-month stability studies for (b) (4) count bottles for the 60 mg and 80 mg TR Tablets with the request for an extrapolated shelf life of 24 months on June 15, 2009. (b) (4) .

The original and revised dissolution specification limits for Oxycodone HCL 10, 15, 20, 30, 40, 60, and 80 are listed in the Table 1.

Product	Dissolution Time	Specification		
		Original	12-month update	24-month update
10, 15, and 20 mg	1st hour	(b) (4)		
	4th hour			
	12th hour	NLT (b) (4)	NLT (b) (4)	NLT (b) (4)
30 and 40 mg	1st hour	(b) (4)		
	4th hour			
	12th hour	NLT (b) (4)	NLT (b) (4)	NLT (b) (4)
60 mg	1st hour			(b) (4)
	4th hour			
	12th hour			NLT (b) (4)
80 mg	1st hour			(b) (4)
	4th hour			
	12th hour			NLT (b) (4)

When the revised specification is used, based on these analyses and evaluations of Oxycodone data, the product is expected to remain within specifications through 24 months for 10, 15, 20, 30, 40, 60, and 80 mg TR tablets. The analysis showed that 24-month expiration was established for 10, 15, 20, 30, 40, 60, and 80 mg TR tablets. However, because there is no data for 60 and 80 mg with 100 counts per package, the shelf-life for 60 and 80 mg with 100 counts per package are not established.

1.2 Overview of the Submission

The sponsor submitted a 24-month stability studies for (b) (4), 100, (b) (4) count bottles of Oxycodone HCL 10, 15, 20, 30 and 40 mg TR Tablets with the request for an extrapolated shelf life of 24 months on May 13, 2009. The sponsor also submitted a 24-month stability studies for (b) (4) count bottles for the 60 mg and 80 mg TR Tablets with the request for an extrapolated shelf life

of 24 months on June 15, 2009. One batch per strength was used in stability studies. Each batch was split into [redacted] package counts, such as [redacted], 100, [redacted] counts per package.

The statistical analyses were not performed for the assay data or the dissolution data at 1 hour, 4 hours, or 12 hours of Oxycodone. The statistical analyses were not performed for degradation data because nearly all of the reported values except a few observations were reported as NMT [redacted]

1.3 Principal Findings

1.3.1 Sponsor's Results and Conclusions

(I) Stability analysis for Oxycodone HCL 10, 15, 20, 30 and 40 mg TR Tablets

In the submission on May 13, 2009, the sponsor tabulated long term stability data up to 24 months for Oxycodone HCL 10, 15, 20, 30 and 40 mg TR Tablets. The sponsor's conclusions were based on the eye-balling the results and specifications:

1. Assay of Oxycodone HCl: all assay results were within the current proposed specification [redacted] label claim) for the long-term 24-month stability data.

2. Degradation products:
[redacted]: observed values were <0.1%.
2) Individual unknown degradation product
All individual unknown degradation products were within the specification limit of NMT [redacted].
From samples at all testing intervals, there were only four cases where the unknown degradation products were observed in levels at or above [redacted] as listed below:
[redacted] in 20 mg, 100 count at 1 month room temperature
in 40 mg, 100 count at 1 month room temperature
in 30 mg, [redacted] count at 12 months room temperature
in 10 mg, [redacted] count at 24 months room temperature
To provide additional information of the unknown in the 30 mg stability sample and to confirm the original data of [redacted] for this unknown, two additional sample solutions of the 30 mg, [redacted] count, 12 months, room temperature stability sample were prepared and analyzed. This unknown in the two retested samples were below the LOD limit of 0.05%.

3). Total degradation Products
The results at all testing intervals (through 24 months at long-term stability) were within the specification (NMT [redacted]) and the values ranged from NMT [redacted]

From samples at all testing intervals, there was only one case where the total degradation products was observed at a level above [redacted] The total degradation products result was [redacted] in the 30 mg, [redacted] count, 12 months room temperature stability sample.

4). Dissolution
All dissolution results from long-term stability data through 24 months met the proposed specifications in Table 1.

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